Washington University in St. Louis

INFORMED CONSENT DOCUMENT

Project Title: Investigation of cerebrospinal fluid (CSF) pharmacokinetics of ondansetron

Principal Investigator: Simon Haroutounian, PhD

Research Team Contact: Karen Frey, 314 454-5980

This consent form describes the research study and helps you decide if you want to participate. It provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights and responsibilities as a research participant. By signing this form you are agreeing to participate in this study.

- You should read and understand the information in this document including the procedures, risks and potential benefits.
- If you have questions about anything in this form, you should ask the research team for more information before you agree to participate.
- You may also wish to talk to your family or friends about your participation in this study.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We invite you to participate in this research study because you are a healthy person and are scheduled to have hip or knee surgery with spinal anesthesia.

The purpose of this research study is find out how much of a drug called ondansetron circulates in your blood and how much circulates in your spinal fluid after it is given IV (intravenously). Ondansetron is an FDA-approved drug that is routinely used to treat nausea and vomiting caused by surgery or cancer treatment. If you choose to participate in this study, the time you will receive this drug before surgery will be determined by the study procedures described below. You may also receive this drug following surgery, if needed for nausea and vomiting, and if considered necessary by your clinical team.

The purpose of this research study is also to see if ondansetron may be potentially helpful in treating people who have pain due to nerve damage. This study will help us understand whether ondansetron reaches the spinal fluid, and the way by which ondansetron may relieve pain from damaged nerves.

Ondansetron is considered investigational, which means that it has not been approved by the U.S. Food and Drug Administration. This is because the 16mg ondansetron dose in this study, which is approved for the prevention of nausea and vomiting after chemotherapy, has not been approved by the U.S. Food and Drug Administration for preventing nausea and vomiting after surgery.

WHAT WILL HAPPEN DURING THIS STUDY?

After you sign the consent, if you have a history of liver or kidney disease, we may do some additional blood tests to make sure you can continue in this study. One sample of 5ml (approximately 1 teaspoon) would be taken for this purpose. These tests will look for things such as liver of kidney failure. If you have a history of any irregular heart rate or rhythm, you may undergo an electrocardiogram (ECG) to

check your heart. An ECG involves electrodes (sticky patches) being attached to your chest, arms and legs to monitor your heart activity while you lay still for a few minutes. If you have not had a pregnancy test, and you are a woman of childbearing potential, you will have a pregnancy urine test to ensure you are not pregnant. These additional tests may be performed at the time of your consent or on the day of surgery.

On the day of your surgery, a research team member will meet you in pre-operative holding area. You may be asked to arrive a little earlier to perform the research study procedures. You will have an IV [intravenous catheter] inserted in each arm. One will be used by your surgical care team to give you fluids and anesthesia during your surgery and the other will be used for collecting blood samples for this research study.

The study drug, ondansetron, will be given to you through the IV as an infusion lasting 15 minutes. This will start at 30, 60 or 120 minutes before your anesthesiologist begins the spinal anesthesia which is your routine care. The timing will be determined by randomization (similar to flipping a coin). A trained member of the research team will collect up to six blood samples from your IV immediately before the ondansetron infusion and at approximately 15, 30, 60, 120 and 180 minutes. Each sample is approximately 1 teaspoon. We will also collect 1 additional teaspoon of blood for genetic analysis to see if your genes play a role in how your body metabolizes ondansetron. Genetic analysis studies your DNA to look for mutations (changes) that may affect the way a person responds to treatment.

A research nurse, who will be with you in the holding area during the study treatment, will be collecting the research blood samples and monitoring your heart rate and blood pressure during the infusion.

Once the spinal needle is inserted for your anesthesia as a part of your routine care, a small sample of your spinal fluid, about 4mL, which is less than a teaspoon, will be collected.

Will you save my research data to use in future research studies?

As part of this study, we are obtaining data from you. We would like to use this data for studies going on right now as well as studies that are conducted in the future. These studies may provide additional information that will be helpful in understanding pain from nerve damage, or other diseases or conditions, including research to develop investigational tests, treatments, drugs or devices that are not yet approved by the U.S. Food and Drug Administration. It is unlikely that what we learn from these studies will have a direct benefit to you. There are no plans to provide financial compensation to you should this occur. By allowing us to use your data, you give up any property rights you may have in the data.

If you change your mind and do not want us to store and use your data for future research you should contact the research team member identified at the top of this document. The data will no longer be used for research purposes. However, if some research with your data has already been completed, the information from that research may still be used. Also, if the data has been shared with other researchers it might not be possible to withdraw the data to the extent it has been shared.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 30 people will take part in this study conducted by investigators at Washington University.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for approximately 3 hours on the day of your surgery. If blood tests or ECG are required, this may add additional 10-15 minutes of involvement.

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

Ondansetron

Likely / Common

Mild

- diarrhea
- constipation
- headache
- dry mouth
- tiredness

Less Likely / Less Common

Mild

- elevated liver function tests, which means the liver may not be functioning properly and can cause fatigue and jaundice (yellowing of the skin and eyes)

Rare

Serious

- Serious irregular heartbeats
- Low potassium in the blood, which can increase the risk of irregular heartbeats
- Fever
- Severe allergic reaction, such as rash, hives, fever, difficulty breathing, and low blood pressure
- Seizures
- Temporary blindness

Intravenous catheter placement

Likely / Common

- Bruising at the site of placement

Rare

- Infection at the site of placement or in the blood stream.

Blood Drawing

The blood draw may cause bleeding, bruising, or pain. Some people become dizzy or feel faint. There is also a rare risk of infection.

Collection of cerebral spinal fluid
Less likely/less common

- Headache after the surgery

ECG
You may develop a mild rash where the electrodes (sticky patches) are attached.

Women Capable of Becoming Pregnant
If you are a woman capable of becoming pregnant, we will ask you to have a pregnancy test before beginning this study. You cannot participate in the study if you are pregnant, as, there may be unknown risks to your unborn child, or risks to your unborn child that we did not anticipate. If you believe or know you have become pregnant while participating in this research study, please contact the research team member identified at the top of this document as soon as possible. Please discuss with the research team how long you need to wait before becoming pregnant after completing the treatment or procedures on this study.

Genetics
There is a federal law called the Genetic Information Nondiscrimination Act (GINA). In general, this law makes it illegal for health insurance companies, group health plans and employers with greater than 15 employees to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance or long term-care insurance.

Breach of Confidentiality
One risk of participating in this study is that confidential information about you may be accidentally disclosed. We will use our best efforts to keep the information about you secure. Please see the section in this consent form titled *"How will you keep my information confidential?"* for more information.

WHAT ARE THE BENEFITS OF THIS STUDY?

You will not benefit from being in this study.

However, we hope that, in the future, other people might benefit from this study if we discover a different therapy for people that suffer from pain due to nerve damage.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You will not have any costs for being in this research study.

You and/or your medical/hospital insurance provider will remain responsible for your regular medical care expenses.

WILL I BE PAID FOR PARTICIPATING?

You will be paid for being in this research study. You will need to provide your social security number (SSN) in order for us to pay you. You may choose to participate without being paid if you do not wish to provide your social security number (SSN) for this purpose. If your social security number is obtained for payment purposes only, it will not be retained for research purposes.

You will receive a $100 Target gift card for being in this research study. You will receive the gift card after the surgery while still in the hospital. If you complete the screening procedure, but cannot participate because of your blood, pregnancy or ECG test results, you will receive a $25 Target gift card.

WHO IS FUNDING THIS STUDY?

The University and the research team are not receiving payment from other agencies, organizations, or companies to conduct this research study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

Washington University investigators and staff will try to reduce, control, and treat any complications from this research. If you feel you are injured because of the study, please contact the investigator Dr. Simon Haroutounian at 314 286-1715 or by pager at 314-419-5583 and/or the Human Research Protection Office at 1-(800)-438-0445.

Decisions about whether payment for medical treatment for injuries relating to your participation in research will be made by Washington University**.** If you need to seek medical care for a research-related injury, please notify the investigator as soon as possible.

HOW WILL YOU KEEP MY INFORMATION CONFIDENTIAL?

We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- Government representatives, (including the Office for Human Research Protections) to complete federal or state responsibilities
- The U.S. Food and Drug Administration
- Hospital or University representatives, to complete Hospital or University responsibilities
- Information about your participation in this study may be documented in your health care records and be available to your health care providers who are not part of the research team.
- The last four digits of your social security number may be used in hospital or University systems to track billing information for research procedures
- Washington University's Institutional Review Board (a committee that oversees the conduct of research involving human participants) and the Human Research Protection Office. The Institutional Review Board has reviewed and approved this study.

To help protect your confidentiality, you will be assigned a study ID number and we will use that ID to manage all your study related information and blood samples. Additionally, the key to the ID code linking code numbers to names will be kept at a separate location, under lock and key, and only the research team will have access to it. We will destroy the link between your ID and your identifiers at the end of the study. If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Are there additional protections for my health information?

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, you must give the research team permission to use and disclose (share) your PHI for the study as explained in this consent form. The research team will follow state and federal laws and may share your health information with the agencies and people listed under the previous section titled, "How will you keep my information confidential?"

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

The research team will only use and share your information as talked about in this form or as permitted or required by law. When possible, the research team will make sure information cannot be linked to you (de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form. If you have questions or concerns about your privacy and the use of your PHI, please contact the University's Privacy Officer at 866-747-4975.

Although you will not be allowed to see the study information, you may be given access to your health care records by contacting your health care provider.

If you decide not to sign this form, it will not affect

- your treatment or the care given by your health provider.
- your insurance payment or enrollment in any health plans.
- any benefits to which you are entitled.

However, it will not be possible for you to take part in the study.

If you sign this form:

- You authorize the use of your PHI for this research
- This authorization does not expire.
- You may later change your mind and not let the research team use or share your information (you may revoke your authorization).
  - To revoke your authorization, complete the withdrawal letter, found in the Participant section of the Human Research Protection Office website at http://hrpo.wustl.edu/participants//withdrawing-from-a-study/ or you may request that the investigator send you a copy of the letter.
    - **If you revoke your authorization:**
      - The research team may only use and share information already collected for the study.
      - Your information may still be used and shared as necessary to maintain the integrity of the research, for example, to account for a participant's withdrawal from the research study or for safety reasons.
      - You will not be allowed to continue to participate in the study.

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. Any data that was collected as part of your participation in the study will remain as part of the study records and cannot be removed.

If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I decide to withdraw from the study?

You may withdraw by telling the study team you are no longer interested in participating in the study or you may send in a withdrawal letter. A sample withdrawal letter can be found at http://hrpo.wustl.edu/participants/ under Withdrawing from a Research Study.

Will I receive new information about the study while participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can someone else end my participation in this study?

Under certain circumstances, the investigator or your doctors might decide to end your participation in this research study earlier than planned. This might happen for no reason or because in our judgment it would not be safe for you to continue.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: Karen Frey at 314 454-5980 or Dr. Simon Haroutounian at 314 286-1715 or by pager at 314-419-5583. If you experience a research-related injury, please contact: Dr. Simon Haroutounian at 314 286-1715 or by pager at 314-419-5583.

If you have questions, concerns, or complaints about your rights as a research participant, please contact the Human Research Protection Office at 660 South Euclid Avenue, Campus Box 8089, St. Louis, MO 63110, 1-(800)-438-0445, or email hrpo@wustl.edu. General information about being a research participant can be found on the Human Research Protection Office web site, http://hrpo.wustl.edu. To offer input about your experiences as a research participant or to speak to someone other than the research staff, call the Human Research Protection Office at the number above.

This consent form is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by agreeing to participate in this study. As a participant you have rights and responsibilities as described in this document and including:

- To be given enough time before signing below to weigh the risks and potential benefits and decide if you want to participate without any pressure from the research team or others.
- To understand all of the information included in the document, have your questions answered, and receive an explanation of anything you do not understand.
- To follow the procedures described in this document and the instructions of the research team to the best of your ability unless you choose to stop your participation in the research study.

- To give the research team accurate and complete information.
- To tell the research team promptly about any problems you have related to your participation, or if you are unable to continue and wish to stop participating in the research study.

Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a signed and dated copy of this form.

Do not sign this form if today's date is after EXPIRATION DATE: 05/03/18.

_____ _____
(Signature of Participant) (Date)

_____
(Participant's name – printed)

Statement of Person Who Obtained Consent

The information in this document has been discussed with the participant or, where appropriate, with the participant's legally authorized representative. The participant has indicated that he or she understands the risks, benefits, and procedures involved with participation in this research study.

_____ _____
(Signature of Person who Obtained Consent) (Date)

_____
(Name of Person who Obtained Consent - printed)